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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,

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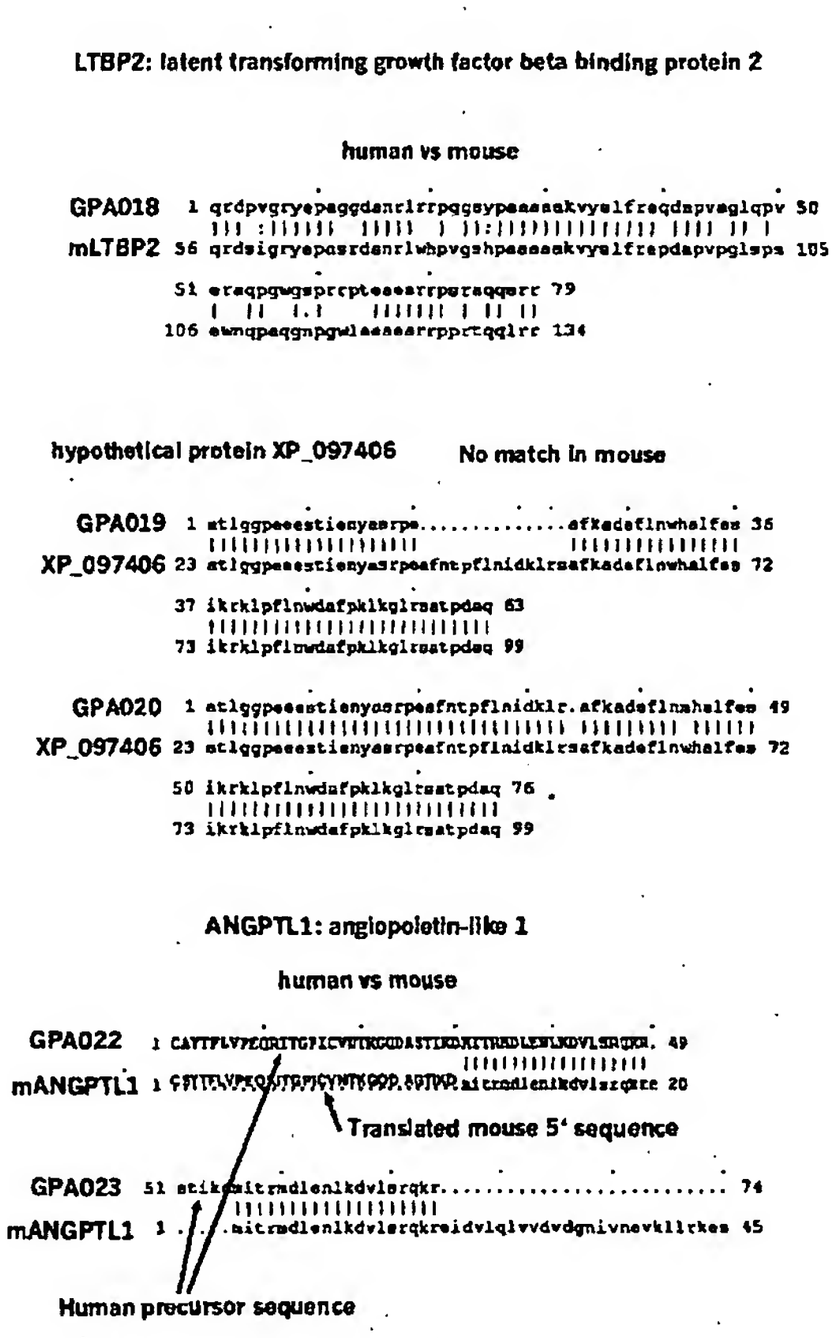
(54) Title: USE OF FIBROBLAST GROWTH FACTOR FRAGMENTS



(57) Abstract: A discovery process beginning with an *in vivo* screening of proteins, peptides, natural products, classical medicinal compound or other substances. The administration of compounds to the animal can be either direct or indirect, such as by the administration and expression of cDNA-containing plasmids. Since the discovery process of the invention is based on a non-preconceived hypothesis and whole organism multi-organ analysis, a compound can be selected for testing in the absence of any biological selection criteria. The resulting organism-wide pattern of the gene expression changes in the transcriptome provides an overview of the activities at the molecular and organism-wide levels. The discovery process of the invention then integrates *in vivo* profiling and internal and external genomic databases to elucidate the function of unknown proteins, typically within few months. The invention further relates to medical uses of fibroblast growth factor 23 (FGF-23), FGF-23 fragments, FGF-23 C-terminal polypeptides, FGF-23 homologs and/or FGF-23 variants.

WO 2005/045044 A3

GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) **Designated States** *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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10 November 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2004/012572

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/19

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE Geneseq 'Online! 28 March 2003 (2003-03-28), "Human fibroblast growth factor 23 polypeptide." XP002316719 retrieved from EBI accession no. GSN:ABP58110 Database accession no. ABP58110 the whole document	18-42
X	WO 02/088358 A (GENEPROT INC.) 7 November 2002 (2002-11-07) the whole document	18-42
X	WO 01/66596 A (CHIRON CORPORATION) 13 September 2001 (2001-09-13) the whole document	18-42

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
8 February 2005	08. 08. 2005

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Novak-Giese, S

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2004/012572

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	JONSSON K.B. ET AL: "Fibroblast growth factor 23 in oncogenic osteomalacia and X-linked hypophosphatemia" THE NEW ENGLAND JOURNAL OF MEDICINE, vol. 348, no. 17, 24 April 2003 (2003-04-24), pages 1656-1663, XP008037462 the whole document	18-42

orm PCT/ISA/210 (continuation of second sheet) (January 2004)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2004/012572

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

18-42

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 18-42

Uses of a polypeptide in the treatment of diseases associated with deregulated angiogenesis, wherein said polypeptide is FGF-23, and variants thereof.
Also encompassed are methods for the treatment of above diseases using said polypeptides, respectively pharmaceutical compositions comprising said polypeptides.

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2. claims: 1-17

(Business) methods for identifying compounds as a candidate in pharmaceutical development

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2004/012572

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 02088358 A	07-11-2002	BR 0209144 A	08-06-2004
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		US 2003105302 A1	05-06-2003